

What is claimed is:

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1. An isolated nucleic acid molecule encoding an odorant receptor protein, wherein the receptor protein comprises seven transmembrane domains, and is further characterized by at least one of the following characteristics:

10 (a) the loop between the first transmembrane domain and the second transmembrane domain, and the second transmembrane domain together comprise consecutive amino acids having the following sequence:

15 -L, X, X, P, M, Y, X, F, L- (SEQ ID NO: 55);

20 (b) the third transmembrane domain, and the loop between the third transmembrane domain and the fourth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-M, X, Y, D, R, X, X, A, I, C- (SEQ ID NO: 57);
or

25 -D, R, X, X, A, I, C- (SEQ ID NO: 59);

30 (c) the loop between the fifth transmembrane domain and the sixth transmembrane domain, and the sixth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

35 -K or R, X, F, S, T, C, X, S, H- (SEQ ID NO: 61); or

-F, S, T, C, X, S, H- (SEQ ID NO: 63); or

(d) the seventh transmembrane domain and the C-terminal domain together comprise consecutive amino acids having one of the following sequences:

-P, X, X, N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 65); or

-P, X, X, N, P, X, I, Y- (SEQ ID NO: 67); or

-N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 69);

wherein X is any amino acid.

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15 2. The isolated nucleic acid molecule of claim 1 wherein:

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(a) the loop between the first transmembrane domain and the second transmembrane domain, and the second transmembrane domain together comprise consecutive amino acids having the following sequence:

-L, H or Q, K or M or T, PMY, F or L, FL- (SEQ ID NO: 56);

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(b) the third transmembrane domain, and the loop between the third transmembrane domain and the fourth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

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-M, A or S, YDR, F or Y, L or V, AIC- (SEQ ID NO: 58); or

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-DR, F or Y, L or V, AIC- (SEQ ID NO: 60);

(c) the loop between the fifth transmembrane domain

and the sixth transmembrane domain, and the sixth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

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-K or R, A or I or S or V, FSTC, A or G or S, SH- (SEQ ID NO: 62); or

-FSTC, A or G or S, SH- (SEQ ID NO: 64); or

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(d) the seventh transmembrane domain and the C-terminal domain together comprise consecutive amino acids having one of the following sequences:

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-P, M or L or V, F or L or V, NP, F or I, IY, C or S or T, LRN- (SEQ ID NO: 66); or

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-P, M or L or V, F or L or V, NP, F or I, IY- (SEQ ID NO: 68); or

-NP, F or I, IY, C or S or T, LRN- (SEQ ID NO: 70).

25 3. The isolated nucleic acid molecule of claim 1, wherein the receptor protein is characterized by at least two of the characteristics (a) through (d).

30 4. The isolated nucleic acid molecule of claim 1, wherein the receptor protein is characterized by at least three of the characteristics (a) through (d).

35 5. The isolated nucleic acid molecule of claim 1, wherein the receptor protein is characterized by all of the characteristics (a) through (d).

6. An isolated nucleic acid molecule encoding an

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odorant receptor protein, wherein the nucleic acid molecule encodes a protein selected from the group consisting of:

- 5 (a) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with tyrosine at position 333 as set forth in row F3 of Figures 4A to 4M (SEQ ID NO: 71),
- 10 (b) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with glutamine at position 313 as set forth in row F5 of Figures 4A to 4L (SEQ ID NO: 72),
- 15 (c) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with lysine at position 311 as set forth in row F6 of Figures 4A to 4L (SEQ ID NO: 73),
- 20 (d) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with glycine at position 317 as set forth in row F12 of Figures 4A to 4L (SEQ ID NO: 74),
- 25 (e) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 310 as set forth in row I3 of Figures 4A to 4L
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- (f) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with glycine at position 327 as set forth in row I7 of Figures 4A to 4L (SEQ ID NO: 76),
- (g) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with tryptophan at position 312 as set forth in row I8 of Figures 4A to 4L (SEQ ID NO: 77),
- (h) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 314 as set forth in row I9 of Figures 4A to 4L (SEQ ID NO: 78),
- (i) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 312 as set forth in row I14 of Figures 4A to 4L (SEQ ID NO: 79),
- (j) an odorant receptor protein comprising consecutive amino acids having a sequence identical to that beginning with methionine at position 1 and ending with leucine at position 314 as set forth in row I15 of Figures 4A to 4L (SEQ ID NO: 80), and

(k) an odorant receptor protein that shares from 40-80% amino acid identity with any one of the proteins of (a)-(j), comprises seven transmembrane domains, and is further characterized by at least one of the following characteristics:

(i) the loop between the first transmembrane domain and the second transmembrane domain, and the second transmembrane domain together comprise consecutive amino acids having the following sequence: -L, X, X, P, M, Y, X, F, L- (SEQ ID NO: 55);

(ii) the third transmembrane domain, and the loop between the third transmembrane domain and the fourth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-M, X, Y, D, R, X, X, A, I, C- (SEQ ID NO: 57); or

-D, R, X, X, A, I, C- (SEQ ID NO: 59);

(iii) the loop between the fifth transmembrane domain and the sixth transmembrane domain, and the sixth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-K or R, X, F, S, T, C, X, S, H- (SEQ ID NO: 61); or

-F, S, T, C, X, S, H- (SEQ ID NO: 63); or

(iv) the seventh transmembrane domain and the

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cont

C-terminal domain together comprise consecutive amino acids having one of the following sequences:

5 -P, X, X, N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 65); or

10 *Sub B3 cont* -P, X, X, N, P, X, I, Y- (SEQ ID NO: 67); or

-N, P, X, I, Y, X, L, R, N- (SEQ ID NO: 69);

wherein X is any amino acid.

15 7. The isolated nucleic acid molecule of claim 6 wherein:

20 (i) the loop between the first transmembrane domain and the second transmembrane domain, and the second transmembrane domain together comprise consecutive amino acids having the following sequence:

25 -L, H or Q, K or M or T, PMY, F or L, FL- (SEQ ID NO: 56);

30 (ii) the third transmembrane domain, and the loop between the third transmembrane domain and the fourth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-M, A or S, YDR, F or Y, L or V, AIC- (SEQ ID NO: 58); or

35 -DR, F or Y, L or V, AIC- (SEQ ID NO: 60);

(iii) the loop between the fifth transmembrane domain and the sixth transmembrane domain, and the sixth transmembrane domain together comprise consecutive amino acids having one of the following sequences:

-K or R, A or I or S or V, FSTC, A or G or S, SH- (SEQ ID NO: 62); or

-FSTC, A or G or S, SH- (SEQ ID NO: 64); or

(iv) the seventh transmembrane domain and the C-terminal domain together comprise consecutive amino acids having one of the following sequences:

-P, M or L or V, F or L or V, NP, F or I, IY, C or S or T, LRN- (SEQ ID NO: 66); or

-P, M or L or V, F or L or V, NP, F or I, IY- (SEQ ID NO: 68); or

-NP, F or I, IY, C or S or T, LRN- (SEQ ID NO: 70).

8. An isolated nucleic acid molecule encoding an odorant receptor protein, wherein the nucleic acid molecule comprises a nucleic acid sequence which can be amplified by polymerase chain reaction using:

(a) any one of 5' primers A1 (SEQ ID NO: 37), A2 (SEQ ID NO: 38), A3 (SEQ ID NO: 39), A4 (SEQ ID NO: 40), or A5 (SEQ ID NO: 41); and

(b) any one of 3' primers B1 (SEQ ID NO: 42), B2 (SEQ ID NO: 43), B3 (SEQ ID NO: 44), B4 (SEQ ID NO: 45), B5 (SEQ ID NO: 46), or B6 (SEQ ID NO: 47).

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9. An isolated nucleic acid molecule encoding an odorant receptor protein, wherein the nucleic acid molecule comprises:

(a) a nucleic acid sequence given in any one of Figures 9 to 31 (SEQ ID Nos: 1-10, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, or 35); or

(b) a nucleic acid sequence degenerate to a sequence of (a) as a result of the genetic code.

10. The isolated nucleic acid molecule of claim 8 or 9, wherein the odorant receptor protein comprises seven transmembrane domains.

11. The isolated nucleic acid molecule of claim 1, wherein the loop between the fifth and sixth transmembrane domains consists of 17 amino acids.

12. The isolated nucleic acid molecule of claim 10, wherein the loop between the fifth and sixth transmembrane domains consists of 17 amino acids.

13. The isolated nucleic acid molecule of any one of claims 1, 6, 8, or 9, wherein the odorant receptor is a vertebrate odorant receptor.

14. The isolated nucleic acid molecule of claim 13, wherein the vertebrate odorant receptor is a fish odorant receptor or a mammalian odorant receptor.

15. The isolated nucleic acid molecule of claim 14, wherein the mammalian odorant receptor is a human odorant receptor, a rat odorant receptor, a mouse odorant receptor or a dog odorant receptor.

16. The isolated nucleic acid molecule of claim 1, 6, 8, or 9, wherein the nucleic acid is DNA.
- 5 17. The isolated nucleic acid molecule of claim 16, wherein the DNA is cDNA.
18. A vector comprising the isolated nucleic acid molecule of claim 1, 6, 8, or 9.
- 10 19. The vector of claim 18, wherein the vector additionally comprises elements necessary for replication and expression in a suitable host.
- 15 20. A purified odorant receptor protein encoded by the isolated nucleic acid molecule of claim 1, 6, 8, or 9.
21. A cell transfected with the vector of claim 19.
- 20 22. The cell of claim 21, wherein the cell is an olfactory cell.
23. The cell of claim 21, wherein the cell is a non-olfactory cell.
- 25 24. The cell of claim 23, wherein prior to being transfected with the vector the non-olfactory cell does not express an odorant receptor protein.
- 30 25. A method of identifying a desired odorant ligand, which comprises contacting a non-olfactory cell of claim 23, which expresses on its cell surface a known odorant receptor, with a series of odorant ligands and determining which ligands bind to the known odorant receptor on the non-olfactory cell.
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26. A method of identifying a desired odorant receptor, which comprises contacting a series of non-olfactory cells of claim 23 with a known odorant ligand and determining which odorant receptor binds with the odorant ligand.
27. A method of detecting an odor which comprises:
- (a) identifying an odorant receptor which binds the desired odorant ligand identified by the method of claim 26; and
 - (b) imbedding the receptor in a membrane such that when the odorant ligand binds with the receptor identified in (a) above, a detectable signal is produced.
28. The method of claim 27 wherein the desired odorant ligand is a pheromone.
29. The method of claim 27 wherein the desired odorant ligand is the vapor emanating from cocaine, marijuana, heroin, hashish, angel dust, gasoline, natural gas, alcohol, decayed human flesh, gun powder, an explosive, a plastic explosive, or a firearm.
30. The method of claim 27 wherein the desired odorant ligand is a toxic fume, a noxious fume or a dangerous fume.
31. The method of claim 27 wherein the membrane is a cell membrane, an olfactory cell membrane, or a synthetic membrane.
32. The method of claim 27 wherein the detectable signal is a color change, a phosphorescence, a

radioactivity, a visual signal, or an auditory signal.

33. A method of quantifying the amount of an odorant
ligand present in a sample which comprises the
method of claim 27 wherein the detectable signal is
quantified.

34. A method of developing fragrances, which comprises
identifying a desired odorant receptor by the method
of claim 26, then contacting a non-olfactory cell,
which has been transfected with an expression vector
comprising an isolated nucleic acid molecule
encoding the desired odorant receptor such that the
receptor is expressed upon the surface of the non-
olfactory cell, with a series of compounds to
determine which compounds bind with the receptor.

35. A method of identifying an odorant fingerprint,
which comprises contacting a series of cells, which
have been transformed such that each express a known
odorant receptor encoded by a nucleic acid molecule
of any one of claims 1, 6, 8, or 9, with a desired
sample containing one or more odorant ligand and
determining the type and quantity of the odorant
ligands present in the sample.

36. A method of identifying a compound which inhibits an
odorant receptor, which comprises contacting an
odorant receptor encoded by the nucleic acid
molecule of any one of claims 1, 6, 8, or 9 with a
series of compounds and determining which compound
inhibits interaction between the odorant receptor
and an odorant ligand known to bind to the odorant
receptor.

37. A method for identifying an appetite suppressant

compound, which comprises identifying a compound by the method of claim 36 wherein the odorant receptor is associated with the perception of food.

- 5 38. A pharmaceutical composition comprising a compound identified by the method of claim 37 and a pharmaceutically acceptable carrier.
- 10 39. A nasal spray for controlling appetite, which comprises a compound identified by the method of claim 37 in a suitable carrier.
- 15 40. A method for controlling appetite in a subject, which comprises administering to the subject an amount of a compound identified by the method of claim 37 effective to control the subject's appetite.
- 20 41. The method of claim 40, which comprises administering the compound to the subject's olfactory epithelium.
- 25 42. A method of trapping odors, which comprises contacting a membrane comprising a plurality of a desired odorant receptor encoded by the nucleic acid molecule of any one of claims 1, 6, 8, or 9 with a sample comprising a desired odorant ligand such that the desired odorant ligand is absorbed by the binding of the odorant ligand to the odorant receptor.
- 30 43. An odor trap, which comprises a membrane comprising a plurality of a desired odorant receptor encoded by the nucleic acid molecule of any one of claims 1, 6, 8, or 9, such that a desired odorant ligand is absorbed by the binding of the odorant ligand to the odorant receptor.
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- 5 44. A method for controlling a pest population in an area, which comprises spraying the area with an odorant receptor ligand identified by the method of claim 25.
45. The method of claim 44, wherein the odorant ligand is an alarm odorant ligand.
- 10 46. The method of claim 44, wherein the odorant ligand interferes with an interaction between an odorant ligand and an odorant receptor associated with fertility.
- 15 47. The method of claim 44, wherein the pest population is a population of rodents, mice, or rats.
- 20 48. A pharmaceutical composition comprising an odorant ligand identified by the method of claim 25 and a pharmaceutically acceptable carrier.
- 25 49. A method of promoting fertility in a subject which comprises administering to the subject an amount of an odorant ligand identified by the method of claim 25 effective to promote the subject's fertility.
- 30 50. The method of claim 49, wherein the odorant ligand interacts with an odorant receptor associated with fertility.
- 35 51. A method of inhibiting fertility in a subject which comprises administering to the subject an amount of an odorant ligand identified by the method of claim 25 effective to inhibit the subject's fertility.
52. The method of claim 51, wherein the odorant ligand inhibits an interaction between an odorant ligand

and an odorant receptor associated with fertility.

53. The method of claim 49 or 51, which comprises administering the odorant ligand to the subject's olfactory epithelium.

54. Use of an odorant ligand identified by the method of claim 25 for the preparation of a pharmaceutical composition for controlling a pest population in a desired area by spraying the desired area with the identified odorant ligand.

55. The use of claim 54, wherein the odorant ligand is an alarm odorant ligand.

56. Use of an odorant ligand identified by the method of claim 25 for the preparation of a pharmaceutical composition for controlling a pest population.

57. The use of claim 56, wherein the odorant ligand interferes with the interaction between odorant ligands and odorant receptors which are associated with fertility.

58. Use of any one of claims 54 to 57 wherein the pest population is a population of rodents, mice, or rats.

59. Use of an odorant ligand identified by the method of claim 25 for the preparation of a pharmaceutical composition for promoting fertility.

60. The use of claim 59, wherein the odorant ligand interacts with odorant receptors associated with fertility.

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